Claims

1. A method of treating a subject having an HCV infection that was not successfully treated using a previous non-CpG therapy comprising

administering to a subject in need of such treatment a CpG immunostimulatory nucleic acid in an amount effective to treat the infection.

2. The method of claim 1, wherein the non-CpG therapy includes interferon-alpha.

3. The method of claim 2, wherein the interferon-alpha is interferon-alpha-2b, interferon-alpha-2a or consensus interferon-alpha.

4. The method of claim 2, wherein the non-CpG therapy includes interferon-alpha and Ribavirin.

5. The method of claim 2, wherein the non-CpG therapy includes pegylated interferon-alpha and Ribavirin.

6. The method of claim 1, wherein the CpG immunostimulatory nucleic acid is an A class CpG immunostimulatory nucleic acid.

7. The method of claim 1, wherein the CpG immunostimulatory nucleic acid is a B class CpG immunostimulatory nucleic acid

8. The method of claim 1, wherein the CpG immunostimulatory nucleic acid is a C class CpG immunostimulatory nucleic acid.

9. The method of claim 1, further comprising the step of administering interferon-alpha to the subject.

10. The method of claim 9, wherein the interferon-alpha is interferon-alpha-2b, interferon-alpha-2a or consensus interferon alpha.

11. The method of claim 9, wherein the interferon-alpha is administered substantially simultaneously with the CpG immunostimulatory nucleic acid.

12. The method of claim 1, wherein the CpG immunostimulatory nucleic acid comprises a backbone modification.

13. The method of claim 12, wherein the backbone modification is a phosphorothioate backbone modification.

14. The method of claim 1, wherein the CpG immunostimulatory nucleic acid comprises a semi-soft backbone.

15. A method of treating a subject having an HCV infection and likely to be non-responsive to a non-CpG therapy comprising

administering to a subject in need of such treatment a CpG immunostimulatory nucleic acid in an amount effective to treat the infection.

16 The method of claim 15, further comprising identifying a subject likely to be non-responsive to a non-CpG therapy.

17. The method of claim 16, wherein the subject is identified as likely to be non-responsive based on an assay of interferon-alpha produced per dendritic cell.

18. The method of claim 16, wherein the subject is identified as likely to be non-responsive based on HCV genotype.

19. The method of claim 15, wherein the non-CpG therapy includes interferon-alpha.

20. The method of claim 15, wherein the non-CpG therapy includes interferon-alpha and Ribavirin.

21. The method of claim 20, further comprising administering to the subject an anti-viral agent.

22. The method of claim 21, wherein the anti-viral agent is interferon-alpha.

23. The method of claim 22, wherein the interferon-alpha is interferon-alpha-2b, interferon-alpha-2a or consensus interferon alpha.

24. The method of claim 21, wherein interferon-alpha administered in a sub-therapeutic amount.

25. The method of claim 15, wherein the CpG immunostimulatory nucleic acid is a C class CpG immunostimulatory nucleic acid.

26. The method of claim 15, wherein the CpG immunostimulatory nucleic acid comprises a semi-soft backbone.

27. A method for screening CpG immunostimulatory nucleic acids useful in the treatment of chronic hepatitis C viral infection comprising

contacting peripheral blood mononuclear cells from a subject having a chronic hepatitis C viral infection, with a CpG immunostimulatory nucleic acid, and

measuring a test response of the blood mononuclear cells after exposure,

wherein the subject was not successfully treated using a previous therapy.

28. The method of claim 27, wherein the test response is selected from the group consisting of B cell stimulation, secretion of IL-6, secretion of IL-10, secretion of IL-12, secretion of interferon-gamma, secretion of type 1 interferons (alpha + beta), secretion of IP-10, NK activity, expression of CD80, expression of CD 86, expression of CD83, and upregulation of class II MHC expression.

29. The method of claim 27, wherein the peripheral blood mononuclear cells comprise dendritic cells.

30. The method of claim 29, wherein the dendritic cells comprise plasmacytoid dendritic cells.

31. The method of claim 29, wherein the test response is selected from the group consisting of secretion of IL-12, secretion of type 1 interferons, expression of CD80, expression of CD 86, expression of CD83, and upregulation of class II MHC expression.

32. The method of claim 29, wherein the contacting occurs in vitro.

33. The method of claim 32, wherein the peripheral blood mononuclear cells are cultured.

34. The method of claim 33, wherein the CpG immunostimulatory nucleic acid is added to the cultured peripheral blood mononuclear cells.

35. The method of claim 29, wherein the previous therapy is a non-CpG therapy.

36. The method of claim 29, wherein the previous therapy is therapy with a CpG nucleic acid of a different sequence or class.

37. The method of claim 29, further comprising screening the CpG immunostimulatory nucleic acid for the ability to stimulate a control response from peripheral blood mononuclear cells from a normal subject.

38. The method of claim 29, further comprising contacting peripheral blood mononuclear cells to interferon-alpha substantially simultaneously with the CpG immunostimulatory nucleic acid.

39. The method of claim 29, wherein the CpG immunostimulatory nucleic acid is a C class CpG immunostimulatory nucleic acid.

40. A method for identifying a subject having an HCV infection and likely to be non-responsive to a non-CpG therapy comprising

exposing peripheral blood mononuclear cells harvested from a subject having a hepatitis C viral infection to a CpG immunostimulatory nucleic acid,

measuring interferon-alpha produced from the cells, and

determining an amount of interferon-alpha produced per dendritic cell, wherein an amount that is below 1.0 pg/ml is indicative of a subject that is likely to be non-responsive to a non-CpG therapy.

41. The method of claim 40, wherein an amount that is below 0.5 pg/ml is indicative of a subject that is likely to be non-responsive to a non-CpG therapy.

42. The method of claim 40, wherein the non-CpG therapy comprises interferon-alpha.

43. The method of claim 42, wherein the non-CpG therapy comprises Ribavirin.

44. The method of claim 42, wherein the IFN-alpha is pegylated interferon-alpha.

45. The method of claim 40, wherein the CpG immunostimulatory nucleic acid is an A class or a C class CpG immunostimulatory nucleic acid.

46. The method of claim 40, wherein the peripheral blood mononuclear cells are further exposed to an anti-viral agent together with a CpG immunostimulatory nucleic acid.

47. The method of claim 46, wherein the anti-viral agent is interferon-alpha.

48. The method of claim 47, wherein interferon-alpha is interferon-alpha-2b, interferon-alpha-2a or consensus interferon alpha.

49. The method of claim 40, wherein the peripheral blood mononuclear cells comprise dendritic cells.

50. The method of claim 49, wherein the dendritic cells comprise plasmacytoid dendritic cells.

51. The method of claim 40, wherein the hepatitis C viral infection is an acute hepatitis C viral infection.

52. The method of claim 40, further comprising determining a genotype of the HCV.

53. A method of treating a subject having a hepatitis C viral infection comprising administering to a subject identified according to the method of claim 40 a CpG immunostimulatory nucleic acid molecule in an amount effective to treat the infection.

54. The method of claim 53, further comprising administering to the subject interferon-alpha.

55. The method of claim 54, wherein the interferon-alpha is interferon-alpha-2b, interferon-alpha-2a or consensus interferon-alpha.

56. The method of claim 53, wherein the CpG immunostimulatory nucleic acid is an A class CpG immunostimulatory nucleic acid.

57. The method of claim 53, wherein the CpG immunostimulatory nucleic acid is a B class CpG immunostimulatory nucleic acid.

58. The method of claim 53, wherein the CpG immunostimulatory nucleic acid is a C class CpG immunostimulatory nucleic acid.

59. The method of claim 53, wherein the CpG immunostimulatory nucleic acid comprises a backbone modification.

60. The method of claim 59 wherein the backbone modification is a phosphorothioate backbone modification.

61. The method of claim 53, wherein the CpG immunostimulatory nucleic acid comprises a semi-soft backbone.

62. The method of claim 53, wherein the hepatitis C viral infection is a chronic hepatitis C viral infection.

63. The method of claim 53, wherein the hepatitis C viral infection is an acute hepatitis C viral infection.

64. A method of treating a subject having an HCV infection that was not successfully treated using a previous non-CpG therapy comprising

administering to a subject in need of such treatment a C class CpG immunostimulatory nucleic acid having a semi-soft backbone in an amount effective to treat the infection.

65. A method of treating a subject having an HCV infection and likely to be non-responsive to a non-CpG therapy comprising

administering to a subject in need of such treatment a C class CpG immunostimulatory nucleic acid having a semi-soft backbone in an amount effective to treat the infection.

66. A method for identifying a subject having an HCV infection and likely to be non-responsive to a non-CpG therapy comprising

exposing peripheral blood mononuclear cells harvested from a subject having a hepatitis C viral infection to a A class or a C class CpG immunostimulatory nucleic acid,

measuring interferon-alpha produced from the cells, and

determining an amount of interferon-alpha produced per dendritic cell, wherein an amount that is below 1.0 pg/ml is indicative of a subject that is likely to be non-responsive to a non-CpG therapy.

67. A method of treating a subject having an HCV infection that was not successfully treated using a previous non-CpG therapy comprising

contacting peripheral blood mononuclear cells from a subject in need of such treatment, with a CpG immunostimulatory nucleic acid in an amount effective to stimulate an immune response, and

re-infusing the cells into the subject.

68. The method of claim 67, wherein the peripheral blood mononuclear cells comprise dendritic cells.

69. The method of claim 68, wherein the dendritic cells comprise plasmacytoid dendritic cells.

70. The method of claim 67, wherein the CpG immunostimulatory nucleic acid is a C class immunostimulatory nucleic acid.

71. The method of claim70, wherein the C class immunostimulatory nucleic acid has a semi-soft backbone.